REMARKS

Claims 45-53 are pending; claim 45-48 have been amended. Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks.

Claim of Priority under 35 U.S.C. §119

Applicants thank the Examiner for acknowledgement of the claim for priority under 35 U.S.C. §119 and receipt of the priority document.

The Objection to Claim 45 for Informalities

Claim 45 was objected to for informalities relating to the alleged clarity of several terms. Applicants have amended the claim to incorporate the Examiner's suggested language. Therefore, Applicants respectfully request that the objections be withdrawn.

The Rejection of Claims 45-53 under 35 U.S.C. §112, 2nd Paragraph

Claims 45-53 were rejected under 35 U.S.C. §112, 2nd paragraph for allegedly indefinite language. Applicants have amended claim 45 to incorporate the language suggested by the Examiner. Therefore, Applicants respectfully request that the rejection be withdrawn.

The Rejection of Claims 45-53 under 35 U.S.C. §112, 1st Paragraph

Claims 45-53 were rejected under 35 U.S.C. §112, 1st paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner has rejected the claims as allegedly containing new matter in the recitation of the

hybridization conditions, that is, 1% SDS. This recitation has been amended to recite 0.1% SDS, as suggested by the Examiner. Therefore, withdrawal of this rejection is respectfully requested.

Claims 45-53 were rejected under 35 U.S.C. §112, 1st paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner alleges that there is no description of a single proline or glutamic acid excreting protein, nor, the Examiner alleges, is there any disclosure of the critical structural elements required in a polynucleotide which hybridizes to the polynucleotide of SEQ ID No. 9 under the claimed conditions. Lastly, the Examiner alleges that there is no disclosure of a method of producing L-lysine, L-proline, or L-glutamic acid using an Escherichia cell wherein the expression of a protein able to excrete proline or glutamic acid is increased.

Applicants respectfully disagree with the above assertions and allegations, and respectfully assert that claimed invention is fully and adequately described by the disclosure. For instance, Examples 3 and 7 in the specification clearly demonstrate the effect of amplification of 3 different plasmids on L-glutamic acid production and L-proline production, respectively. The claimed gene YahN, contained in one of the exemplified plasmids, clearly has an effect in that an increase in glutamic acid and proline production is seen in tables 2 and 7, respectively.

The Examiner states that no disclosure is made of a single proline or glutamic acid excreting protein; however, as Examples 3 and 7 clearly indicate, the YahN gene encodes a protein that enables excretion of L-glutamic acid and L-proline. Therefore, the Examiner's statement is directly contradictary to the data presented in the Examples. It is also noted production of glutamic acid and proline does not necessarily lead to the

presence of a single proline or glutamic acid excreting protein. In fact, although the excreted amounts depend on the properties of the parent strain, the three amino acids are inherently produced in the medium of Examples 3 and 7. One skilled in the art would be able to select the L-amino acid desired to be recovered from the medium.

Furthermore, in the specification, amino acid excreting genes and their corresponding proteins are described and identified by their SEQ ID No. in the paragraph bridging pages 8 and 9. SEQ ID No. 10 is clearly described as a protein capable of the activity of enabling excretion of L-glutamic acid, L-lysine, and L-proline. Also, clearly a method has been described for producing L-lysine, L-proline, and L-glutamic acid using an E. coli wherein the expression of a protein able to excrete L-proline or L-glutamic acid is increased, as this is the exact method which is described in Examples 3 and 7.

The Examiner asserts that the structure of a proline or glutamic acid exreting protein is completely undefined. This is a wholly incorrect assertion in that Examples 3 and 7, as well as the paragraph bridging pages 8 and 9 identify and adequately describe SEQ ID No. 10, and describe a method for using this protein to enable excretion of proline and glutamic acid. Furthermore, one of ordinary skill in the art would be able based upon the conditions recited in the claim and the description in the specification to determine hybrids to the nucleotide defined by SEQ ID No. 9 that would have the same activity as the protein depicted in SEQ ID No. 10. Determination and isolation of hybrids under the stated conditions involves experiments well within the skill of the ordinarily skilled artisan, and therefore, entails no undue experimentation. A representative number of species has been presented in the Examples in the specification since one can easily,

and without undue experimentation, determine whether a species will fall within the genus or not.

The Examiner has also rejected claims 45-53 under 35 U.S.C. 112, 1st paragraph for being non-enabling for a method wherein the E. coli cell has been modified such that any proline or any glutamic acid excreting protein is increased. Again, this assertion is directly contradicted by the data presented in Examples 3 and 7. As stated above, the specification is clearly enabling for the amino acid excreting proteins which enable excretion of L-lysine, L-glutamic acid, and L-proline, particularly the protein described in Examples 3 and 7, that is the YahN protein.

Based on these arguments, Applicants assert that the rejections under 35 U.S.C. §112, 1st paragraph are improper and should be withdrawn. Applicants respectfully request action to this effect.

Rejection of the claims under 35 U.S.C. §103

The Examiner has rejected the claims under 35 U.S.C. §103(a) as allegedly being unpatentable over Blattner in view of Vrljic and Kojima. The Examiner has asserted that Blattner teaches that the polypeptide is a transmembrane protein, and that it belongs to the lysE protein family based on structural homology. The Examiner acknowledges that Blattner does not teach increased expression of the polypeptide to enhance amino acid production. The Examiner alleges that Vrljic and Kojima make up for this deficiency by teaching isolation of C. glutamicum lysE gene and the characterization of the protein product as a lysine transporter protein, and a method of producing L-lysine by using a mutated (multi-copy vector) aspartokinase III transformed cell.

Applicants respectfully disagree with the Examiner's allegations. Applicants argue that in view of the knowledge in the art at the time of the present invention, the invention was not obvious over the teachings of the asserted combined references. In particular, Blattner's suggestion is entirely insufficient, combined with the other references and the knowledge in the art at the time, to render the present invention as currently claimed, obvious.

As evidence of the state of the art at the time of the present invention, applicants submit the reference, *J. Mol. Microbiol. Biotechnol.* (1999) 1(2):327-336 (copy attached). This reference describes that the LysE family is related to the YahN and CadD families, and that the three families comprise the LysE superfamily (abstract, lines 15-21). However, among the families, there is little to no homology between the genes. The only shared property is the presence of the hydrophobic regions.

The reference describes the YahN family members in Table 2. Again, at the protein level, only four residues are fully conserved, and the only areas that are well-conserved are the hydrophobic domains (see p. 334, 1st full paragraph). The common characteristic to the members of this family is that they are membrane proteins, but that the functions of the different protein members of the family are different.

Turning to the CadD family from S. aureus, also identified in the reference as a member of the LysE superfamily, the reference also describes cadium resistence as a functional common trait. As can be readily seen, this function is very different from the functions described for LysE.

This reference thus demonstrates that even within the same superfamily having members with a common number of hydrophobic regions, the members did not always

have the same function. At the time of the present invention, therefore, even if Blattner's suggestion that the polypeptide of SEQ ID No. 10 is a lysE homolog, one skilled in the art could not reasonably have expected that YahN would have a function similar to that of LysE.

For these reasons, applicants respectfully submit that the claimed invention is not obvious of the art of record. Applicants respectfully request that the Examiner re-consider the claimed invention in light of the comments set forth above, and withdraw the rejection.

Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Ramirez believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, she is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned respectfully requests that she be contacted immediately.

Att'y Dkt. No. US-127O

U.S. App. No: 09/459,573

Respectfully submitted,

By: _____
Shelly Guest Cermak
Registration No. 39,571

USPTO Customer No. 38108
Ajinomoto USA, Inc.
1120 Connecticut Ave.
Ste. 101
Washington D.C. 20036

202 457 0284

Date: